





Lisa Medley/DC/USEPA/US

01/03/2006 11:15 AM

TO NCIC HPV@EPA

2006 JAH 13 AH 11: 40

CC

bcc

Subject Fw: HPV test plan and robust summaries - dimethyl

disulfide

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---- Forwarded by Lisa Medley/DC/USEPA/US on 01/03/2006 11:15 AM -----



Ann TVEIT <ann.tveit@arkemagroup.c om>

12/31/2005 12:15 PM

TO NCIC OPPT@EPA, Rtk Chem@EPA

cc Sandi MURPHY <sandi.murphy@arkemagroup.com>

Subject HPV test plan and robust summaries - dimethyl disulfide

Attached please find the test plan and currently available robust study summaries for dimethyl disulfide, (CAS# 624-92-0) which Arkema Inc volunteered to sponsor in the HPV program in a letter dated October 21, 2005. The test plan and robust study summaries will be updated as additional information becomes available.

If you have any questions please feel free to contact me. My contact information is listed below.

Thanks

Ann

Ann Tveit, Ph.D., DABT Arkema Inc 2000 Market St. Philadelphia, PA 19103 phone 215-419-5604 fax 215-419-5800





email ann.tveit@arkemagroup.com dmds-hpv.pdf test plan dmds.pdf

201-16161A

High Production Volume (HPV) Challenge Program

DIMETHYL DISULFIDE (CAS# 624-92-0) Test Plan OPPER STREET BOOK OF THE BOOK

Arkema Inc. 2000 Market Street 19103 Philadelphia, PA

December 2005

EXECUTIVE SUMMARY

Arkema Inc has volunteered to sponsor dimethyl disulfide (DMDS, CAS# 624-92-0) in the USEPA HPV program. The DMDS Test Plan is being submitted to fulfill the United States Environmental Protection Agency (USEPA) High Production Volume (HPV) Challenge Program commitment for DMDS.

Data from company proprietary files, peer-reviewed literature, and/or calculated endpoints using widely accepted computer modeling programs have been identified for purposes of this program. Robust summaries of the available data are included in the attached IUCLID. The following table summarizes the available data and proposed testing for DMDS.

Table 1: Matrix of Available and Adequate Data on DMDS

"SIDS ENDPOINT"	Data Available Y/N	Testing Planned? Y/N
Physical and Chemical Data		
Melting Point	Υ	N
Boiling Point	Υ	N
Vapor Pressure	Υ	N
Partition Coefficient	Υ	N
Water Solubility	Υ	N
Environmental Fate		
Photodegradation	Υ	N
Stability in Water (Hydrolysis)	N	Y
Transport/Distribution	Y	N
Biodegradation	Y	N
Ecotoxicity		
Acute/Prolonged Toxicity to Fish	N	Y
Acute Toxicity to Aquatic Invertebrates (Daphnia)	Y	N
Acute Toxicity to Aquatic Plants (Algae)	Y	N
Toxicity		
Acute Toxicity (Oral)	Υ	N
Acute Toxicity (Dermal)	Y	N
Acute Toxicity (Inhalation)	Υ	N
Repeated Dose	Υ	N
GeneticToxicity in vitro – Gene Mutation	Y	Ν
Genetic Toxicity in vitro— Chromosomal Aberration	Y	N
Reproductive Toxicity Developmental Toxicity	Y	N

Note: The data used to characterize the OECD SIDS endpoints for substances in this Test Plan were identified either in company proprietary files, peer-reviewed literature, and/or calculated using widely accepted computer modelling programs. All data were evaluated for study reliability in accordance with criteria outlined by the USEPA (1999a). Only studies that met the reliability criteria of "1" (reliable without restrictions) or "2" (reliable with restrictions) were used. Additional data are also included in the IUCLID (International Uniform Chemical Information Dataset) attached in Annex I. A more detailed discussion of the data quality and reliability assessment process used to develop this test plan is provided in Annex II.

1.1 Physico-Chemical properties

DMDS is a pale yellow liquid with a strong garlic like odor. Experimental data for the physical chemical parameters are available and reported in EPIWIN[©] (USEPA, 2004) and are provided in the following table.

Table 2.	Physicochemical Data

Parameter	Value
Melting Point	-85°C ¹
Boiling Point	110°C ¹
Vapor Pressure	29.3 hPa
Kow Partition Coefficient	1.77
Water Solubility (mg/l)	2500 ¹

¹EPIWIN v3.12 – Syspro database

Conclusion

Adequate data are available for the HPV physical/chemical property endpoints. No additional testing for the HPV program is proposed.

GENERAL INFORMATION ON EXPOSURE

1.2 Production Volumes and Use Pattern

DMDS is on EPA's high production volume list indicating it is manufactured and/or imported at greater than 1 million pounds per year according to the toxic inventory update rule (IUR).

1.2.1 Use Pattern:

DMDS has several industrial uses. It is used in the oil industry as a sulfiding/presulfiding agent to activate catalysts of hydrotreating units, to reduce the number of decoking operations in the petrochemical industry, as a chemical intermediate in the fine chemical industry, and as an anti-corrosive in metallurgy.

1.3 Environmental Exposure and Fate

1.3.1 Photodegradation

The photodegradation of DMDS was evaluated using EPIWIN 3.12. The half life of DMDS was calculated to be 0.565 hours based on the experimental rate constant of 227 x E-12 cm3/molecule-sec.

Conclusion

Adequate data are available to assess the photodegradation of DMDS. No additional studies are proposed for the HPV program.

1.3.2 Stability in Water

EPIWIN was unable to calculate a hydrolysis rate for DMDS. A hydrolysis study is proposed for DMDS.

1.3.3 Transport between Environmental Compartments

The transport of DMDS between environmental compartments was assessed by fugacity modeling using EPIWIN (v3.12). Results are listed in the table below:

Table 3. Fugacity Results for DMDS

Compartment	Mass amount (%)	Estimated half life (hr)
Air	1.01	1.13
Water	58.1	360
Soil	40.8	360
Sediment	0.168	3.24x e003

1.3.4 Biodegradation

DMDS was not readily biodegradable when evaluated according to OECD 301D. The degradation was less than 10% following 28 days exposure.

Conclusion

Adequate data are available to assess the biodegradation of DMDS. No additional studies are proposed for the HPV program.

2 HUMAN HEALTH HAZARDS

2.1.1 Acute Toxicity

Single exposure (acute) studies indicate DMDS is moderately toxic if swallowed (rat; 290 mg/kg < LD50 < 500 mg/kg), no more then slightly toxic if absorbed through skin (rabbit LD50 >2,000 mg/kg), and slightly toxic if inhaled (rat 4-hr LC50 805 ppm).

Conclusion

Adequate data are available to assess the acute toxicity of DMDS and no additional studies are proposed.

2.1.2 Repeated Dose Toxicity

DMDS was evaluated in a 90-day repeated dose study on rats according to OECD guidelines. This study featured inhalation dosing, measurement of mortality, body weight changes, food consumption, hematological and blood biochemical examinations, urinalysis, organ weights, histopathology and a functional observational battery. Rats were exposed whole body to 0, 10, 50, 150, and 250 ppm DMDS for 6 hours per day for 90 days. Satellite groups were evaluated

following a 2-week recovery period. Results from this study showed decreased body weights, food consumption, hypoactivity, changes in white blood cell counts, reduced thymus gland weight and increased liver weight. Reversible microscopic changes were noted in the nasal mucosa.

Conclusion

Adequate data are available to assess the reproductive toxicity of DMDS. No additional testing is proposed for purposes of the HPV program.

2.1.3 Mutagenicity

Several reliable genetic toxicity studies are available for DMDS. Predominantly negative results were obtained with DMDS when tested *in vitro* (negative bacterial and mammalian mutagenicity assays, negative DNA damage and repair, ambiguous positive in vitro chromosome aberration study using human lymphocytes). Negative results were obtained when DMDS was evaluated *in vivo* (mouse micronucleus, unscheduled DNA synthesis).

Conclusion

Adequate data are available to assess the genetic toxicity of DMDS. No additional testing is proposed for purposes of the HPV program.

2.1.4 Toxicity for Reproductive/Developmental Toxicity

Reproductive Toxicity

The 90 day repeated dose toxicity study will be used to assess the reproductive toxicity of DMDS. Reproductive organs examined in this study included the epididymus, prostate, and testes in males and ovaries and uterus in females. No lesions were reported.

Developmental Toxicity

A Developmental Toxicity test was completed for DMDS in Sprague-Dawley rats following OECD Guideline 414 "Teratogenicity." DMDS was administered by inhalation to 0, 5, 15, and 50 ppm on gestation days 6 to 15. Maternal toxicity was noted at 15 and 50 ppm. No evidence of developmental toxicity was observed. No additional studies are proposed.

Conclusion

Adequate data are available to assess the reproductive and developmental toxicity of DMDS. No additional testing is proposed for the HPB program.

3 HAZARDS TO AQUATIC O RGANISMS

DMDS has been evaluated in an acute daphnia immobilization and algal growth inhibition studies. DMDS is moderately toxic to daphnia with a 48 hour EC50 value of 7 mg/l. DMDS is slightly toxic to *Selenastrum capricornutum* alga with a 72 hour EC50 of 35 mg/l. No data are available for acute fish and alga. No data are available to assess the acute fish toxicity and an acute fish toxicity (OECD guideline 203) is proposed for DMDS.

Conclusion

Adequate data are available to assess the aquatic toxicity of DMDS to daphnia and alga but not fish. An acute fish toxicity study is proposed (OECD guideline 203) for DMDS.

References

Atofina, 2005. IUCLID Data Set, CAS No. 624-92-0 dimethyldisulfide. Atofina, Paris, France.

Klimisch, H.J., E. Andreae, and U. Tillmann. 1997. A systematic approach for evaluating the quality of experimental and ecotoxicological data. *Reg. Tox. and Pharm*. 25: 1-5.

Organisation for Economic Co-operation and Development (OECD) Secretariat. 2002. *Manual for Investigation of HPV Chemicals* (November 2002).

U.S. Environmental Protection Agency (USEPA), Office of Pollution Prevention and Toxics. 1998. Guidance for Meeting the SIDS Requirements: Chemical Right-to-Know Initiative.

USEPA, Office of Pollution Prevention and Toxics. 1999b. Draft Determining the Adequacy of Existing Data.

USEPA, Office of Pollution Prevention and Toxics and Syracuse Research Corporation. 2004. EPI Suite v 3.12.

ANNEX I: DIMETHYL DISULFIDE IUCLID

See attached IUCLID documents.

ANNEX II: DATA QUALITY ASSESSMENT

Available environmental, ecotoxicity, and mammalian toxicity studies were reviewed and assessed for reliability according to standards specified by Klimisch et al., (1997), as recommended by the USEPA (1999a) and the OECD (OECD, 2002). The following reliability classification (Klimisch rating) has been applied to each study assessed:

- 1 = Reliable without Restriction Includes studies that comply with USEPA- and/or OECD-accepted testing guidelines and were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented;
- 2 = Reliable with Restriction Includes studies that were conducted according to national/international testing guidance and are well documented. May include studies that were conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance; also includes studies with test parameters that are well documented and scientifically valid but vary slightly from current testing guidance. Also included in this category were physical-chemical property data obtained from reference handbooks, as well as environmental endpoint values obtained from an accepted method of estimation (e.g., USEPA's EPIWIN estimation program);
- 3 = Not Reliable Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or in which documentation is insufficient; and,
- 4 = Not Assignable This designation is used in this dossier for studies that appear scientifically valid but for which insufficient information is available to adequately judge robustness.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this dossier. Those key studies selected for inclusion are considered typical of the endpoint responses observed in other studies of a similar nature and design that were identified during our search of the literature.

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IUCLID

Data Set

Existing Chemical

CAS No.

: ID: 624-92-0 : 624-92-0

EINECS Name

: dimethyl disulphide

EC No.

: 210-871-0

TSCA Name

: Disulfide, dimethyl

Molecular Formula

: C2H6S2

Producer related part

Company **Creation date** : ATOFINA Chemicals Inc.

: 27.12.2005

Substance related part

Company Creation date : ATOFINA Chemicals Inc.

: 27.12.2005

Status Memo

Printing date

: 31.12.2005

Revision date

Date of last update

: 31.12.2005

Number of pages

: 51

Chapter (profile) Reliability (profile) : Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10 : Reliability: without reliability, 1, 2, 3, 4

Flags (profile)

: Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

ld 624-92-0 **Date** 31.12.2005

1.0.1 APPLICANT AND COMPANY INFORMATION

Type : manufacturer Name : ARKEMA

Contact person

Date

Street : 4-8, cours Michelet La Défense 10
Town : 95091 Paris La Défense Cedex

Country : France

Phone : +33 1 49 00 80 80

Telefax : Telex : Cedex :

Cedex : Email : Homepage :

Source : Atofina Paris La Défense Cedex

14.12.2005

Type : importer of product Name : ARKEMA Chemicals Inc.

Contact person

Date

Street : 2000 Market Street
Town : Philadelphia
Country : United States

Phone

Telefax Telex

Telex Cedex

Email Homepage

Remark: formerly ATOFINA Inc.

Source : Atofina Paris La Défense Cedex

31.12.2005

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name Smiles Code

Molecular formula : C2-H6-S2 Molecular weight : 94.2

Petrol class

Source : Atofina Paris La Défense Cedex

23.12.2005

ld 624-92-0 **Date** 31.12.2005

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance

Substance type : organic Physical status : liquid

Purity : > 99.5 % w/w
Colour : Light yellow
Odour : Strong garlic odour

Source : ARKEMA, Paris-la-Défense, France (JFR)

Atofina Paris La Défense Cedex

23.12.2005

1.1.2 SPECTRA

1.2 SYNONYMS AND TR ADENAMES

DMDS

2,3-Dithiabutane
Dimethyl disulfide
Dimethyldisulfide
Disulfide, dimethyl
Methyldisulfide
Methyldithiom ethane

Source : ARKEMA, Paris-la-Défense, France Atofina Paris La Défense Cedex

27.12.2005

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial

Category : Chemical industry: used in synthesis

ld 624-92-0 **Date** 31.12.2005

Source : Atofina Paris La Défense Cedex

23.12.2005

Type of use : industrial

Category : other: Sulphurization agent (Petrochemical)

Source : ARKEMA, Paris-la-Défense, France (JFR)

Atofina Paris La Défense Cedex

23.12.2005

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

Type : EINECS **Additional information** : 210-871-0

Source : Atofina Paris La Défense Cedex

23.12.2005

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Id 624-92-0 **Date** 31.12.2005

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

Type of search Chapters covered : Internal and External: 3, 4, 5: 23.12.2005 Date of search

: ARKEMA, Paris-la-Défense, France (JFR) Atofina Paris La Défense Cedex Source

23.12.2005

1.13 REVIEWS

ld 624-92-0 **Date** 31.12.2005

2.1 MELTING POINT

Value : -85 °C

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

27.12.2005 (18)

Value : = -84.7 °C

Sublimation : Method : Year :

GLP : no data

Test substance

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

15.11.1993 (28)

2.2 BOILING POINT

Value : = 109.6 °C at 1013 hPa

Decomposition : yes **Method** :

Year :

GLP : no data

Test substance :

Remark : Start of Decomposition: 390 degree C

Decomposition products: Hydrogen sulphide, Dimethyl

sulphide and methanethiol

Similar result (109.6C) reported in Epiwin 3.12 syspro experimental

database

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

31.12.2005 (28)

2.3 DENSITY

Type : density

Value : = $1.063 \text{ g/cm}^3 \text{ at } 20 \text{ °C}$

Method

Year

GLP : no data

Test substance

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

15.11.1993 (28)

2.3.1 GRANULOMETRY

ld 624-92-0 **Date** 31.12.2005

2.4 VAPOUR PRESSURE

Value : = 29.3 hPa at 20 °C

Decomposition

Method

Year

GLP : no data

Test substance

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Reliability : (2) valid with restrictions

:

Flag : Critical study for SIDS endpoint

27.12.2005

Value : = 38 hPa at 25 °C

Decomposition

Method

Year

Year GLP

Test substance :

Source : Atofina, Paris-la-Défense, France.

no data

Atofina Paris La Défense Cedex

15.11.1993 (28)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water Log pow : = 1.77 at °C

pH value

Method : other (measured)

Year

GLP

Test substance : no data

Source: Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

31.12.2005 (20)

Partition coefficient : octanol-water Log pow : = 1.87 at °C

pH value

Method : other (calculated)

Year

GLP

Test substance :

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

04.12.2001 (31)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water

ld 624-92-0 **Date** 31.12.2005

Value : = 2500 mg/l at 20 °C

pH value

concentration : at °C

Temperature effects

Examine different pol.

pKa : at 25 °C

Description Stable

Deg. product Method

Year

GLP : no data

Test substance

Remark: Unit of water solubility: ppm

Similar data (3000 mg/l) reported in EPIWIN v3.12 experimental database

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

31.12.2005 (32)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : = 16 °C

Type : closed cup

Method : other

Year GLP

: no data

Test substance

Remark : Method: ASTM D 93

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

15.11.1993 (28)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

Result : flammable

Method :

Year

GLP : no data

Test substance

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

15.11.1993 (28)

2.10 EXPLOSIVE PROPERTIES

ld 624-92-0 **Date** 31.12.2005

Result : other

Method

:

Year

GLP : no data

Test substance

Remark : Explosive limits of vapours: 1.1 to 16.1 %v/v in air

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

15.11.1993 (28)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

ld 624-92-0 **Date** 31.12.2005

3.1.1 PHOTODEGRADATION

Type : air Light source :

Light spectrum : nm

Relative intensity : based on intensity of sunlight

INDIRECT PHOTOLYSIS

Sensitizer : OH

Conc. of sensitizer

Rate constant : = .000000000227 cm³/(molecule*sec)

Degradation : = 50 % after .6 hour(s)

Result : AOP Program (v1.91) Results:

SMILES: S(SC)C

CHEM: Disulfide, dimethyl MOL FOR: C2 H6 S2 MOL WT: 94.19

----- SUMMARY (AOP v1.91): HYDROXYL RADICALS ------

Hydrogen Abstraction = 2.1216 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 225.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings = 0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant = 227.1216 E-12 cm3/molecule-sec

HALF-LIFE = 0.047 Days (12-hr day; 1.5E6 OH/cm3)

HALF-LIFE = 0.565 Hrs

----- SUMMARY (AOP v1.91): OZONE REACTION------

****** NO OZONE REACTION ESTIMATION ******
(ONLY Olefins and Acetylenes are Estimated)

Experimental Database Structure Match:

Chem Name: Dimethyl disufide CAS Number: 000624-92-0

Exper OH rate constant : 227 E-12 cm3/molecule-sec Exper OH Reference: KWOK,ESC & ATKINSON,R (1994)

Exper Ozone rate constant: --- cm3/molecule-sec Exper NO3 rate constant: 7 E-13 cm3/molecule-sec

Reliability : (2) valid with restrictions

Acceptable calculation method based on experimental rate constant.

Flag : Critical study for SIDS endpoint

31.12.2005

3.1.2 STABILITY IN WATER

Type : abiotic t1/2 pH4 : at °C t1/2 pH7 : at °C t1/2 pH9 : at °C

Remark: Hydrolysis at ambient temperature and pH<12 is too slow to

be an important environmental fate process.

ld 624-92-0 **Date** 31.12.2005

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

27.12.2005 (7)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III

Media

Air : 1.01 % (Fugacity Model Level I)

Water : 58.1 % (Fugacity Model Level I)

Soil : 40.8 % (Fugacity Model Level I)

Biota : % (Fugacity Model Level II/III)

Soil : .165 % (Fugacity Model Level II/III)

Method : other: model

Year

Result : Level III Fugacity Model (Full-Output):

Chem Name : Disulfide, dimethyl

Molecular Wt: 94.19

Henry's LC: 0.00121 atm-m3/mole (Henry database) Vapor Press: 24.5 mm Hg (Mpbpwin program)

Log Kow : 1.77 (Kowwin program) Soil Koc : 24.1 (calc by model)

Mass Amount Half Life Emissions

 (percent)
 (hr)
 (kg/hr)

 Air
 1.01
 1.13
 1000

 Water
 58.1
 360
 1000

 Soil
 40.8
 720
 1000

 Sediment
 0.165
 3.24e+003
 0

Fugacity Reaction Advection Reaction Advection (atm) (kg/hr) (kg/hr) (percent) (percent)

Air 9.37e-012 2.21e+003 36.1 73.8 1.2

Water 1.34e-008 400 208 13.3 6.93

Soil 1.17e-007 141 0 4.69 0

Sediment 1.2e-008 0.126 0.0118 0.00421 0.000394

Persistence Time: 119 hr Reaction Time: 130 hr Advection Time: 1.47e+003 hr Percent Reacted: 91.9 Percent Advected: 8.14

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):

Air: 1.131

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Water: 360 Soil: 720 Sediment: 3240

Biowin estimate: 2.991 (weeks

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

31.12.2005 (19)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic

Inoculum

Contact time

Degradation : < 10 (±) % after 28 day(s) **Result** : other: not readily biodegradable

Kinetic of testsubst. : 7 day(s) = .3 %

14 day(s) = 1.1% 20 day(s) = 1.9%28 day(s) < 0%

%

Control substance : Benzoic acid, sodium salt Kinetic : 14 day(s) = 86.1 %

28 day(s) = 84.5 %

Deg. product : not measured

Method : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"

Year : 1992 **GLP** : no

Test substance: as prescribed by 1.1 - 1.4

Result : O2 dissolved (mg/l)

0 d 7 d 14 d 20 d 28 d

1- Medium + inoculum

mean 8.41 8.26 8.12 7.64 7.32

2- Medium + inoculum + test substance

mean 8.42 8.24 8.05 7.51 7.44

3- Medium + inoculum + test substance + reference substance

mean 8.37 5.55 5.43 4.79 4.74

4- Medium + inoculum + reference substance mean 8.41 2.61 2.37 2.09 1.68

BOD (O2 mg/mg substance)

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0d 7d 14d 20d 28d

serie 2 (substance) 0.00 0.01 0.02 0.04 -0.04

serie 3 (inhibition

control) 0.00 0.76 0.76 0.80 0.73 serie 4 (reference) 0.00 1.41 1.44 1.39 1.41

BIODEGRADATION (%)

0 d 7 d 14 d 20 d 28 d

serie 2 (substance) 0 0.3 1.1 1.9 -1.8

serie 3 (inhibition

control) 0 40.1 39.9 42.2 38.2

serie 4 (reference) 0 84.5 86.1 83.1 84.5

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Reliability : (2) valid with restrictions

Guideline study without detailed documentation.

Flag : Critical study for SIDS endpoint

31.12.2005 (8)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static

Species : Daphnia magna (Crustacea)

Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 7
EC50, 24 h : > 13.4
Analytical monitoring : yes

Method : OECD Guide-line 202

Year : 1996 **GLP** : yes

Test substance : other TS: DMDS, Atofina, 98.93% purity

Result : - Biological observations

20 daphnia per concentration

mg/l	%lm	nmo					
nomin	al	1	2	3	4	total	
13.4	85	1	1	0	1	3	
10.6	75	1	2	1	1	5	
9.5	70	2	2	1	1	6	
7.8	60	3	2	2	1	8	
6.3	50	3	2	3	2	10	
5.5	45	3	3	3	2	11	
4.7	20	4	4	4	4	16	
3.8	10	4	5	4	5	18	
3.3	10	5	5	4	4	18	
0 témo	oin 10	0	5	4	5	4	18

- EC50, 48h: 7 mg/l; 95% CI: 6.5 - 7.6 mg/l

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : - Test organisms

Daphnia magna Straus Clone A from INERIS, France. Breeding colony realized in the laboratory in an Elendt M7 medium, supplemented with algal based feed. Organisms are selected

by sieving

Age at study initiation : < 24h old, laboratory bred

- A stock solution is prepared before the beginning of the test, by mixing 100 mg of the substance with 1 liter of dilution water.

Test temperature range: 20-21°C

Exposure vessel type:

Closed flasks (120 ml) as test glassware entirely filled

with test solutions and stoppered with PTFE bungs and sealed

with aluminum caps.

-Dilution water is prepared in the laboratory using pure

water and salts according to ISO 6341.

25 ml/l of the below solutions, aerated up to oxygen

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saturated

11.76 g CaCl2, 2 H2O /l ultrapure water 4.93 g MgSO4, 7 H2O /l ultrapure water 2.59 g NaHCO3 /I ultrapure water 0.23 g KCI /I ultrapure water

- Dilution water chemistry According to ISO 6341

Ca+Mg ions = 2.5 mmol/l.

Ca/Mg = 4Na/K = 10 $pH 7.8 \pm 0.2$

- incubation of test flasks in darkness.
- Water chemistry in test :

C nominal

(mg/l) 0 3.3 4.0 4.8 5.8 6.9 8.3 10.0 12.0 14.4

02 at 48h (mg/l)

8.3 8.2 8.2 8.3 8.3 8.3 8.4 8.3 8.3

pH at 48 h

7.89 7.90 7.88 7.88 7.95 7.93 7.96 8.01 8.03 8.00

- Test design

Concentration

Nomina	al	Meas	Measured			
	Initial	Final	Final/Initial			
	mg/l	mg/l	%			
3.3	3.3	3.6	109.1			
4.0	3.8	4.1	107.9			
4.8	4.7	5.2	110.6			
5.8	5.5	5.3	96.4			
6.9	6.3	6.6	104.8			
8.3	7.8	8.2	105.1			
10	9.5	9.9	104.2			
12	10.6	11.8	111.3			
14.4	13.4	13.7	102.2			

- Analytical monitoring Gas chromatography/FID

- 5 individuals per replicate (1) valid without restriction

Reliability Flag : Critical study for SIDS endpoint

27.12.2005 (10)

Type static

Species Daphnia pulex (Crustacea)

: no data

Exposure period 4 hour(s) Unit mg/l **EC50** = 21.4**Analytical monitoring** : no Method other Year 1963 **GLP** : no

Test substance

Method : Groups of 3-5 daphnia were dispensed into glass sample

vials, each of which containing 5.0 ml of a biological

harmless "culture water" at 21°C.

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15.0 ml of toxic solution were added.

The vials were transported in the darkness of a covered, thermostatically controlled water-bath (21+-0.05°C).

The vials were set up in triplicate.

There were 6 concentrations per chemical.

The concentration series was progressively adjusted so as to

approach the 50% mortality.

Controls were included in each experiments to give an

estimate of control-mortality.

Source : Atochem Paris la Defense

Atofina Paris La Défense Cedex

04.12.2001 (33)

Type : static

Species : Daphnia pulex (Crustacea)

Exposure period 48 hour(s) Unit mg/l **EC50** = 4 EC50, 24h = 15 **Analytical monitoring** no Method other Year : 1970 **GLP** nο Test substance no data

Remark : Method according to: WERNER, A.E.: Sulphur compounds in

kraft pulp mill effluents.Can. Pulp paper Ind., 1963, 16, 3,

35-43.

Source : Atochem Paris la Defense

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Atofina Paris La Défense Cedex

Test condition: The test was made in glass cylinder of 110 ml capacity. The

volume of the test solution was 100 ml. The temperature was

about 20°C.

04.12.2001 (29)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)

Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/l

 NOEC
 : = 10.43 measured/nominal

 EC10
 : = 9.3 measured/nominal

 EC50
 : = 35 measured/nominal

Limit test

Analytical monitoring : yes

Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"

Year : 2000 GLP : ves

Test substance : other TS: DMDS, Atofina, 99.65% purity

Result : - Values (mg/l)

ErC50, 72h = 35 ErC10, 72h = 9.3 EbC50, 72h = 11 EbC10, 72h = 10.43

NOECb: 10.43 NOECr: 10.43

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- control response satisfactory : yes
- BIOLOGICAL OBSERVATIONS

+Cell density at each flask at each measuring point

Sample Mg/I	e N° T0	Replicat T24h	T48h	algal conc. (Cell/ml) T72h
nom 0	mean	1.00E+04	5.00E+04	2.34E+05 3.28E+06
100	mean	1.00E+04	8.33E+03	2.00E+044.23E+04
55.56	mean	1,00E+04	9.00E+03	3.57E+042.00E+05
30.86	mean	1.00E+04	1.80E+04	1.08E+056.97E+05
17.15	mean	1.00E+04	3.30E+04	2.32E+05 1.68E+06
9.53	mean	1.00E+04	1.60E+04	2.63E+051.91E+06
5.29	mean	1.00E+04	4.50E+04	2.87E+07 2.35E+06

+Percent biomass/growth rate inhibition per concentration

	mean Inhibition %	
sample	integral blomass	growth rate

nominal (mg/l)

	IAI (%)	lµi (%
0	0.00	0.00
5.29	22.03	5.78
9.53	35.27	9.36
17.15	40.10	11.55
30.86	76.32	26.74
55.56	93.70	48.29
100	98.71	75.09

Source

: Atofina, Paris-la-Défense, France. Atofina Paris La Défense Cedex

Test condition

- : Static test
 - · Test temperature range : 24 ± 1 °C
 - · Growth/test medium chemistry

Prepared according to § 1.6.1.2 of C.3. method (Annex 5 of 92/69/EEC Directive)

8 Hq

- · Dilution water source
- See above
- · Exposure vessel type

120 ml glass bottles completely filled with test solution and stoppered with PTFE bungs and sealed with aluminum caps

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(9)

· Water chemistry in test (pH and O2 dissolved mg/l))

C% vol	I TO	T72h	T0	T72h
0	7.31	7.67	7.7	11.2
5.29	7.03	7.46	7.4	10.0
9.53	7.01	7.46	7.5	11.1
17.15	7.00	7.43	7.8	10.7
30.86	7.00	7.36	7.5	9.6
55.56	7.00	7.27	7.6	9.4
100	7.09	7.18	8.1	8.4

· Stock solutions preparation

Ultrapure water (ultrafiltration, active carbon, ions exchange, $0.22~\mu m$ filter) Stock solution prepared 1 h before the beginning of the test, by adding 94 μ l of substance in 1 l of dilution water, stirred during 1h.

- Light levels and quality during exposure Constantly illuminated between 6000 to 10000 lx.
- Test design
- 3 replicates at each test concentration
- 7 concentrations (nominal):

0, 5.29, 9.53, 17.15, 30.86, 55.56,100 mg/l

Reliability Flag 31.12.2005 : (1) valid without restriction: Critical study for SIDS endpoint

31.12.2005

- 4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA
- 4.5.1 CHRONIC TOXICITY TO FISH
- 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES
- 4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS
- 4.6.2 TOXICITY TO TERRESTRIAL PLANTS
- 4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS
- 4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES
- 4.7 BIOLOGICAL EFFECTS MONITORING

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4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type : LD50

Value : 290 - 500 mg/kg bw

Species : rat

Strain : Sprague-Dawley
Sex : male/female

Number of animals : 60

Vehicle : other: polyethylene glycol 300

Doses : 0, 100, 290, 350, 500 and 5300 mg/kg

Method : Directive 84/449/EEC, B.1 "Acute toxicity (oral)"

Year : 1986 GLP : yes Test substance : other TS

Method : DIMETHYL DISULFIDE was administered undiluted at a volume of 5 ml/kg

bw, or as a suspension (10 ml/kg) in polyethylene glycol 300 at the dose

levels of 100, 170, 290, 350 and 500 mg/kg.

Clinical signs, mortality and body weight gain were checked

for a period of up to 14 days following the single

administration of the test item. All animals were subjected

to necropsy.

Result : Mortality:

- 100 and 170 mg/kg: none

- 290 mg/kg : 30 %- 350 mg/kg : none- 500 mg/kg : 100 %

Clinical signs:

Sedation, hypotonia, dyspnea, piloerection and coma,

appeared just after the administration and disappeared after 24 hours.

Body weight:

No effect was noted on the body weight gain of the surviving

rats.

Macroscopic examination:

Haemorragic stomachs was observed at the macroscopic examination of the rats dead on the first day (290 and 500

mg/kg).

Source: ARKEMA, Paris-la-Défense, France (JFR).

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

- Adaptation period: 7 days

- Number of animals: 5 males + 5 females / dose

- Controls: no

HOUSING

The animals were housed 5 of the same sex per polycarbonate

cages

ADMINISTRATION:

- Exposure route: gavage

- Volume administered: see freetext ME

- Post dose observation period: 14 days

EXAMINATIONS: clinical observations, body weight, mortality

and necropsy

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Purity: no data

Conclusion: The oral LD50 of DIMETHYL DISULFURE in rats is lower than

500 mg/kg but higher than 290 mg/kg.

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS

endpoint

31.12.2005

Type : LD50

Value : = 190 mg/kg bw

Species: ratStrain: WistarSex: male/female

Number of animals : 50 Vehicle : CMC

Doses : 125, 188, 250, 375 and 500 mg/kg **Method** : other: EPA 40 CFR 163.81-1

Year

GLP : yes Test substance : other TS

Method : DIMETHYL DISULFIDE w as administered as a suspension in 3%

carboxymethyl cellulose at the dose levels of 125, 188, 250, 375 and 500

mg/kg.

Clinical signs, mortality and body weight gain were checked

for a period of up to 14 days following the single

administration of the test item. All animals were subjected

to necropsy.

Result	: Group	Dose	Mortali	ity	Mortality %
		g/kg	Male	Femal	е
	1	0.125	0/5	1/5	10
	2	0.188	5/5	1/5	60
	3	0.250	3/5	4/5	70
	4	0.375	5/5	5/5	100
	5	0.50	5/5	5/5	100

LD50 = 0.19 (0.15 - 0.24) g/kg

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

- Adaptation period: 14 days

- Number of animals: 5 males + 5 females / dose

- Controls: no

ADMINISTRATION:

- Exposure route: gavage

- Volume administered: no data

- Post dose observation period: 14 days

EXAMINATIONS: clinical observations, body weight, mortality

and necropsy

STATISTICAL DETERMINATION OF THE LD50:

- Litchfield-Wilcoxon method of probit analysis.

Test substance: Test substance: D imethyl disulfide

C AS no.: 624-92-0

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Purity: no data

Conclusion: Acute Oral Defined LD50: 0.19 g/kg

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

31.12.2005 (26)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC50 **Value** : = 805 ppm

Species : rat

Strain : Sprague-Dawley
Sex : male/female

Number of animals : 100

Vehicle

Doses : 0, 500, 700, 775, 800, 840, 875, 950, 1100 and 1581 ppm

Exposure time : 4 hour(s)

Method : other: comparable to OECD Guide-line 403

Year

GLP : no Test substance : other TS

Result: MORTALITY:

See the attached table

CLINICAL SIGNS:

No data

MACROSCOPIC OBSERVATION:

No data

LC50 = 805 (776-835) ppm

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Aldrich Batch: no data Purity: no data

Test substance : TEST ORGANISMS:

- Adaptation period: >= 7 days

- Number of animals: 5 males + 5 females

- Controls: no

HOUSING

The animals of the same sex were housed 5 per cage

ADMINISTRATION:

- Exposure : whole-boby inhalation

- Analytical control of the concentration: no data

EXAMINATIONS:

- Clinical observations, mortality and necropsy

- Post dose observation period: 14 days

STATISTICAL DETERMINATION OF THE LC50:

- Litchfield-Wilcoxon method of probit analysis.

Attached document : Tansy table.bmp

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| Deep | Decides | Decides

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

31.12.2005 (21)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD0

Value : >= 2000 mg/kg bw

Species : rabbit

Strain : New Zealand white

Sex : male/female

Number of animals : 10

Vehicle : other: none Doses : 2000 mg/kg

Method : other: EPA 40 CFR 163.81-2

Year

GLP : yes Test substance : other TS

Method : Adaptation period of at least 7 days,

five male and five female rabbits.

A non-permeable patch containing 2 g/kg body weight of the test material (applied neat) was placed over a 4 -5 cm2 area

on each rabbit.

After 24 hours exposure to the test material, the patches were removed

and the exposed surface was wiped clean of any residual test material using a damp cloth. The rabbits were observed for gross toxicity and mortality at least twice daily for a period of 14 days. Since there were no mortalities, gross necropsies were performed on all

survivors at terminal sacrifice. The body weights were recorded on the day

of dosing and at 7 and 14

days.

Result : All rabbits appeared active and healthy throughout the test

period. There were no overt signs of gross toxicity nor was there any evidence of severe skin lesions. Eight rabbits gained weight over the 14 day observation period and two

remained the same.

Gross necropsies were unrevealing. All organs and tissues

appeared normal.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

- Adaptation period: at least 7 days

- Number of animals: 5 males + 5 females

- Controls: no

ADMINISTRATION:

- Exposure route: dermal, under a non-permeable patch, over

10% of the body surface

- Volume administered: no data

EXAMINATIONS:

- Clinical observations, body weight, mortality and necropsy

- Post dose observati on period: 14 days

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Pennwalt Corp.

Batch: no data Purity: no data

Conclusion : The acute dermal toxicity of Dimethyl Disulfide is > 2.0

g/kg body weight.

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS

endpoint

31.12.2005 (25)

Type : LD0

Value : >= 2000 mg/kg bw

Species : rabbit

Strain : New Zealand white
Sex : male/female

Number of animals : 10

Vehicle: other: noneDoses: 2000 mg/kg

Method : other: Directive 79/831/EEC Annexe V

Year

GLP : no Test substance :

Result: No mortality was observed. Apathy and prostration were noted in most of

the animals between 15 minutes and 3 hours after the application of the

product. An increase in the

spontaneous activity was noted for some animals the first day of treatment. The behavior of the animals during the remainder of the period of observation was considered

normal. No macroscopic lesion was observed.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

- Acclimatation period: no data

- Number of animals: 5 males + 5 females

- Controls: no

ADMINISTRATION:

- Exposure route: dermal, under a non-permeable patch, over

10% of the body surfaceVolume administered: no data

EXAMINATIONS:

- Clinical observations, body weight, mortality and necropsy

- Post dose observation period: 15 days

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: SNEA(P)

Batch: A1 Purity: no data

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

31.12.2005

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species: rabbitConcentration: undilutedExposure: SemiocclusiveExposure time: 4 hour(s)

Number of animals : Vehicle : PDII :

Result : slightly irritating
Classification : not irritating

Method : OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"

Year : 1982 GLP : no Test substance : other TS

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test substance : DMDS, purity 98.98%. **Reliability** : (2) valid with restrictions

Flag : Material Safety Dataset, Directive 67/548/EEC

31.12.2005 (15)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)

Number of animals : 6 Vehicle :

PDII : 1.1

Result : slightly irritating
Classification : not irritating

Method : other: EPA 40 CFR 163.81-5

Year

GLP : yes Test substance :

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

- Adaptation period: 8 weeks

- Number of animals: 4 males + 2 females

- Controls: no

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Pennwalt Corp.

Batch: no data Purity: no data

Conclusion : Based on the average Primary Skin Irritation Score at 48

hours (2.02) and the average score over 14 days (1.10), Dimethyl Disulfide is considered to be a mild primary skin

irritant.

Reliability : (1) valid without restriction

31.12.2005 (23)

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5.2.2 EYE IRRITATION

Species rabbit Concentration undiluted Dose .1 ml **Exposure time** 24 hour(s) not rinsed Comment

Number of animals 6 Vehicle

Result irritating Classification irritating

Method OECD Guide-line 405 "Acute Eye Irritation/Corrosion"

Year 1982 **GLP** nο Test substance other TS

Result Mean scores (24+48+72 hours) for the 6 rabbits:

> -Chemosis: 1.89 -Enanthema: 1.33 - Iris: 1.0. - Cornea: 0.83

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test substance DMDS, purity 98.98%. Reliability (2) valid with restrictions

Flag Material Safety Dataset, Directive 67/548/EEC

31.12.2005 (15)

rabbit Species Concentration undiluted .1 ml Dose

Exposure time

Comment other: not rinsed for 6 rabbits, rinsed after 20-30 sec. for 3 rabbits

Number of animals Vehicle

Result slightly irritating Classification not irritating

Method other: EPA-40 CFR 163-81-4

Year

GLP yes

Test substance as prescribed by 1.1 - 1.4

Result : The average 24 hour maximum mean total score (MMTS) for the

unwashed eyes was 14.8 (minimally irritating.). For the washed eyes the 24 hour MMTS was 6 (minimally irritating).

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

- Adaptation period: 7 days

- Number of animals: 4 males + 5 females

- Controls: no

Conclusion : Dimethyl Disulfide is considered to be minimally irritating

to both the unwashed and the washed eye.

: (1) valid without restriction Reliability

31.12.2005 (22)

SENSITIZATION 5.3

Type : Buehler Test Species : guinea pig

Concentration : 1st: Induction undiluted occlusive epicutaneous

2nd: Challenge undiluted occlusive epicutaneous

3rd:

Number of animals : 20

Vehicle

Result : not sensitizing Classification : not sensitizing

Method : other: EPA-40 CFR 163-81-6

Year : 1985 GLP : yes Test substance :

Result: In the preliminary screen, no erythema was observed at any

of the concentrations of test material applied to the skin over a 48 hour period. The test material was therefore tested neat in the full scale sensitization study.

After the initial and second challenge applications, the

guinea pigs did not exhibit any erythema and were considered non-

sensitized.

Expected responsed were noted in the positive control animals. The data

validates the responsiveness of the guinea pigs to DNCB.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition: TEST ORGANISMS:

- guinea pigs

- Weight at study initiation: 256-424 g

- Adaptation period: 10 days

- Number of animals:

10 males for the test substance

10 males for the positive control (DNCB 0.3%)

METHOD

- Induction: 10 applications every 2 days (excluding

week-end)

duration of the application: 6 hours/dayChallenge test: 10 days after the last induction

pplication

- Scoring local reaction: 24 and 48 hours after each induction application and after the challege application

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Pennwalt Corp.

Batch: no data Purity: no data

Conclusion: Dimethyl Disulfide is a non (contact) sensitizer.

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Directive 67/548/EEC

30.12.2005 (24)

5.4 REPEATED DOSE TOXICITY

Type : Species : rat

Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation

Exposure period : 90 days

Frequency of treatm. : 6 h/day; 5 d/week

Post exposure period : 4 weeks

Doses : 10, 50, 150, 250 ppm **Control group** : yes, concurrent vehicle

NOAEL : ca. 10 ppm **LOAEL** : = 50 ppm

Method : OECD Guide-line 413 "Subchronic Inhalation Toxicity: 90-day Study"

Year : 1981 GLP : yes Test substance :

Method : Four groups of 20 male and 20 female Sprague - Dawley were

exposed 6 hours/day, 5 days/week to 0, 10, 50, 150, or 250 ppm DMDS. The exposure of the 150 ppm group was terminated after 6 weeks and its treatment-free subgroup necropsied 2 weeks later. The remaining groups received a 13 week

exposure period followed by four weeks for the

treatment-free subgroups.

Result : MORTALITY

There was no treatment-related mortality.

CLINICAL SIGNS

The only clinical signs attributable to treatment were salivation, lacrimation or reduced activity during exposure

1 and 2 of the 150 and 250 ppm groups and a low incidence of dyspnoea

or wheezing in the early part of the study, particularly in the 250 ppm animals at week 1.

FOB

Functional observation tests indicated no evidence of neurotoxicity.

BOBY WEIGHT

There was a dosage-related decrease in body weight gain over the treatment period in treated groups compared with

controls.

FOOD CONSUMPTION

Differences in food consumption paralleled those of body

weight gain and werenot statistically significant in the 50 ppm males or the

10 ppm groups.

OPHTHALMOSCOPY

The eyes of the animals were unremarkable.

HAEMATOLOGY

Haematological profiles suggested a possible small reduction in Hb, RBC and PCV in the 250 ppm female group only.

BOOLD CHEMISTRY

Blood chemistry examinations showed treatment-related changes in ALT, alkaline phosphatase and bilirubin.

ORGAN WEIGHTS

There were no changes in organ weights that were considered to be treatment-related.

MACROSCOPIC OBSERVATIONS

There were no treatment-related macroscopic abnormalities at necropsy.

MICROSCOPIC OBSERVATIONS

In the 10, 50 and 250 ppm animals examined microscopically

there was a dose-related effect on nasal mucosa.

: Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

Source

- Number of animals: 100 rats: 20 males + 20 females /

dose group (4 dose groups + 1 control group)

- Aclimatation period: 14 days

ADMINISTRATION:

- Type of inhalation study: whole body

- Production of test atmospheres:

Five horizontal flow, recirculating exposure chambers were used.

- Vehicle: filtered air

- Exposure chamber test article concentration

* Measured concentration

Samples for analysis were withdrawn from the exposure chambers twice hourly.

SATELLITE GROUPS: none

RECOVERY GROUPS

10 rats/sex/group were allowed to recover for 4 weeks after termination of the main study animals in groups 1, 2, 3 and 5 and for 2 weeks for group 4 animals.

CLINICAL OBSERVATIONS AND FREQUENCY:

- Clinical observations
- * Morbidity and mortality
- * Clinical signs
- * Functional observation tests
- * Body weight
- * Food consumption
- * Ophthalmoscopy
- Laboratory investigations
- * Haematology:

Haemoglobin, mean cell volume, red blood cell count and indices: mean cell haemoglobin, mean cell haemoglobin concentration packed cell volume, total and differential white blood cell count platelet count.

* Clinical chemistry:

aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, sodium, potassium, chloride, calcium inorganic phosphorus, glucose, urea, total bilirubin, creatinine, total protein, albumin, albumin/globulin ratio total cholesterol.

- Pathology
- * Necropsy

Full internal and external examination at sacrifice

- * Organ weights
- * Histology
- Statistical evaluation
- * ANOVA, T-test

Body weight: week 0

* ANOVA, Regression and Dunnett's

* ANCOVA, Dunnett's

* Kruskal-Wallis, Terpstra-Jonckheere, Wilcoxon

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Atochem Purity: 99.88%

Conclusion : Clear treatment-related effects were seen at 50 and 250 ppm

and were present to a marginal degree at 10 ppm. It was concluded that the effect level was 50 ppm. The no effect level was in the region of, but less than, 10 ppm due to the

reversible changes in the nasal mucosa

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Critical study for SIDS endpoint

31.12.2005 (11)

Type :

Species: rabbitSex: male/femaleStrain: New Zealand white

Route of a dmin. : dermal Exposure period : 28 days Frequency of treatm. : 6 h/day Post exposure period : no

Doses : 0.01, 0.1, 1 ml/kg/day (10.63, 106.3 and 1063 mg/kg bw/d)

Control group : other: sham treated with the occlusive dressing

NOAEL : = 10.63 mg/kg bw **LOAEL** : = 106.3 mg/kg bw

Method : OECD Guide-line 410 "Repeated Dose Dermal Toxicity: 21/28-day Study"

Year : 1981 GLP : yes Test substance :

Method : DMD S was administered daily, by dermal occlusive application (6 hours

daily) to four groups of albino rabbits. The dose levels equivalent to 0, 10.63, 106.3, and 1063 mg/kg body weight/day, respectively. The control and 1.0 ml/kg/d group consisting of 10 males and 10 females, and the 0.01 and 0.1 ml/kg/d group consisting of 5 males and 5 females. The animals of the 0.01 and 0.1 ml/kg/d group were treated five days a week during a fourweek period, whereas animals of the 1 ml/kg/d group were treated with

DMDS for 2 1/2 weeks (i.e. 13 days of treatment).

Result : CLINICAL SIGNS:

During daily treatment with DMDS, lethargy was observed in a dose related manner in the mid and high dose group. No treatment related clinical signs were observed in the animals of the low dose group or in the controls.

MORTALITY:

During the second and third week of the study

treatment-related mortality occurred in males and females of high dose group and treatment was suspended after 13 days of treatment.

SKIN REACTIONS:

Repeated demal administration of DMDS caused severe, dose-dependent skin irritation in all dose groups.

BLOOD EXAMINATIONS:

Haematology and clinical chemistry examinations revealed differences in some blood paremeters and clinical chemistry in the high dose group males. No treatment related changes were observed in females.

PATHOLOGY:

The absolute and relative organ weights measured at autopsy did not show statistically significant differences. Macroscopic examination

at autopsy did not reveal any treatment-related changes other than the

dermal lesions induced during the treatment with DMDS.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

- Number of animals: The control and top-dose group comprised 10 males and 10 females, whereas the low - and

 $\,$ mid-dose group comprised 5 males and 5 females.

- Aclimatation period: 13 days

ADMINISTRATION:

- Route: dermal

Doses were applied by volume. The respective amounts of the test substance were applied topically to the intact, shaven skin. The test site was covered with porous gauze

dressing fixed onto a non-irritating tape. The entire trunk

was wrapped to maintain the gauze dressing in position and to retard

evaporation of volatile substances.

The animals of the control group were sham-treated with the patches only.

CLINICAL OBSERVATIONS AND FREQUENCY:

- Clinical signs: twice a day on exposure days and once a day on non-exposure days.
- Mortality: twice a day.
- Dermal reactions:

At the start of the study and prior to each daily administration.

- Body weight:
- Food consumption:
- Blood examinations:

haematology and clinical chemistry determinations were conducted in blood or plasma of the animals

* Haematology:

Hemoglobin, hematocrit, red blood cell count, white blood cell count, differential leukocyte count, platelet count, mean cell volume, mean cell haemoglobin concentration, mean cell haemoglobin

- * Biochemistry:
- . Electrolytes: calcium, chloride, phosphorous, potassium, sodium
- . Enzymes: alkaline phosphatase, alanine-aminotransferase, aspartate-aminotransferase, gamma-glutamyl-transferase . Other: albumin, blood creatinine, blood urea nitrogen,
- albumin/globulin, glucose, total bilirubin, total cholesterol, total serum protein, bile acids

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):

- Weighed organs: adrenals, brain, heart, kidneys, liver, lungs, ovaries, spleen, testes, thyroid and thymus.

Microscopic examinations:

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Sourœ: Atochem Purity: 99.88%

Conclusion : The NOAEL of DMDS for systemic toxicity is 10.63 mg/kg bw/d. For local

skin effects, the NOAEL is lower than 10.63 mg/kg bw/d.

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Critical study for SIDS endpoint

31.12.2005 (6)

Type :

Species: rabbitSex: male/femaleStrain: New Zealand white

Route of admin. : dermal Exposure period : 14 days Frequency of treatm. : 6 h/day Post exposure period : no

Doses : 0.1, 0.5 and 1 ml/kg/day (106, 503 and 1063 mg/kg/day)

Control group : other: sham treated with the occlusive dressing

NOAEL : < .1 mg/kg **LOAEL** : = .1 mg/kg

Method : other: range finding study

Year :

GLP : yes Test substance : other TS

Method : In this range -finding study, DMDS was administered to a

restricted number of albino rabbits by dermal occlusive application, daily, during a two-week period. The dose

levels applied were 106.3, 531.5, and 1063 mg DMDS/kg body weight/day,

repectively, and the daily exposure

period was 6 hours. The control group was sham treated with

the occlusive dressing only.

Result : During exposure temporary signs slight lethargy in the low-dose group,

distinct lethargy in

the mid-dose group, and unconscinousness in the high-dose

group. At the end of each daily exposure, these effects were no longer

observed.

During the entire test period of the study, the controls did not show any signs of abnormal beha viour after treatment with the patches only. Repeated dermal administration of DMDS caused severe skin lesions in all three dose groups.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Atochem Purity: 99.88%

Reliability : (1) valid without restriction

31.12.2005 (17)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Salmonella typhimurium reverse mutation assay
System of testing : Strains: TA 1535, TA 1537, TA 1538, TA 98, TA 100

Test concentration : 0, 5, 50, 150, 500, 1500, and 5000 µg/plate

Cycotoxic concentr. : >= $5000 \mu g/plate$ Metabolic activation : with and without

Result : negative

Method : OECD Guide-line 471

Year : 1983 GLP : yes Test substance :

Method : PRELIMINARY TOXICITY ASSAY

The preliminary toxicity assay was used to establish the dose range over which the test article would be assayed.

MUTAGENICITY ASSAY

- Five dose levels of test article along with appropriate vehicle control and positive controls were plated with overnight cultures of TA98, TA100, TA1535, TA1537 and TA1538 on selective agar in the presence and absence of Aroclor induced rat liver S9. All dose levels of test article, vehicle control and positive controls were plated in triplicate.
- Second mutation test

The procedure was repeated at a later date.

EVALUATION OF RESULTS

The mean number of revertant colonies for all treatment groups is compared with those obtained for negative and positive control groups. The effect of metabolic activation is assessed by comparing the results obtained both in the presence and absence of the liver microsomal fraction for each treatment group.

A compound is deemed to provide evidence of mutagenic potential if (1) a statistically significant dose related increase in the number of revertant colonies is obtained in two separate experiments, and (2) the increase in the number of revertant colonies is at least twice the concurrent solvent control value.

Remark Source

Test condition

- : The positive controls responded as expected.
- : Atofina, Paris-la-Défense, France. Atofina Paris La Défense Cedex

: CONTROL MATERIALS

- Negative: culture medium
- Solvent: Dimethylsulphoxide
- Positive:
- * With S-9 mix
- 2-Aminoanthracene at 2 μ g/plate for strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100.
- * Without S-9 mix
- 2-Nitrofluorene at 10 μ g/plate for strains TA 1538 and TA 98.

9-Aminoacridine at 20 μg/plate for strain TA 1537. Sodium azide at 5 μg/plate for strains TA 1535 and TA 100.

ACTIVATION

- S9 derived from Sprague -Dawley rats induced with a single intraperitoneal injection of Aroclor 1254, 500 mg/kg, five days prior to sacrifice.
- S9 mix composition:

Component Concentration
S9 10% (v/v)
Sodium phosphate buffer (pH 7.4) 100 mM
gluc ose 6 -phosphate 5 mM
N ADP 4 mM
KCI 33 mM
MgCl2 8 mM

TEST ORGANISMS

- Salmonella typhimurium strains: TA98, TA100, TA1535, TA1537 and a 1538
- test organisms were properly maintained and were checked for appropriate genetic markers (rfa mutation, R factor)

TEST CONCENTRATIONS

(a) Preliminary cytotoxicity assay:

Plate incorporation assay: 0, 5, 50, 500 and 5000 μg per

plate were evaluated with and without S9 activation in all strains. A single plate was used, per dose, per condition.

(b)Mutation assays:

Plate incorporation assay: 50, 150, 500, 1500 and 5000 µg per plate were evaluated in triplicate in the presence and absence of S9 activation: all test strains were used.

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Purity 98.98%

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Critical study for SIDS endpoint

30.12.2005

Type : Salmonella typhimurium reverse mutation assay System of testing : Strains: TA 1535, TA 1537, TA 1538, TA 98, TA 100

Test concentration : 50, 166, 500, 1666, 5000 µg/plate

Cycotoxic concentr. : 5000 µg/plate

Metabolic activation : with and without

Result : negative

Method : OECD Guide-line 471

Year : 1983 GLP : yes Test substance :

Method : PRELIMINARY TOXICITY ASSAY

The preliminary toxicity assay was used to establish the dose range over which the test article would be assayed.

MUTAGENICITY ASSAY

- Five dose levels of test article along with appropriate vehicle control and positive controls were plated with overnight cultures of TA98, TA100, TA1535, TA1537 and TA1538 on selective agar in the presence and absence of Aroclor induced rat liver S9. All dose levels of test article, vehicle control and positive controls were plated in triplicate.

- Second mutation test

The procedure was repeated at a later date.

TEST PROCEDURE

- Without metabolic activation

0.1 ml aliquots of bacterial suspension is added to each of one set of sterile tubes.

0.1 ml of the test compound is added to cultures at five concentrations. The negative control is the chosen solvent.

The appropriate positive control is also included.

- With metabolic activation

Methodology is as described above except that 0.5 ml of liver homogenate S-9 mix is added to the tubes in place of sterile buffer.

EVALUATION OF RESULTS

The mean number of revertant colonies for all treatment groups is compared with those obtained for negative and positive control groups. The effect of metabolic activation is assessed by comparing the results obtained both in the presence and absence of the liver microsomal fraction for each treatment group.

A compound is deemed to provide evidence of mutagenic potential if (1) a statistically significant dose-related increase in the number of revertant colonies is obtained in

two separate experiments, and (2) the increase in the number

of revertant colonies is at least twice the concurrent

solvent control value.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : CONTROL MATERIALS

- Negative: culture medium

- Solvent: Dimethylsulphoxide

- Positive: * With S-9 mix

2-Aminoanthracene at 5 $\mu g/plate$ for strains TA 1535, TA

1537, TA 1538, TA 98 and TA 100.

* Without S-9 mix

2-Nitrofluorene at 5 $\mu g/plate$ for strains TA 1538 and Ta98

9-Aminoacridine at 150 µg/plate for strain TA 1537.

Sodium azide at 10 µg/plate for strains TA 1535 and TA 100.

ACTIVATION

- S9 derived from Sprague -Dawley rats induced with a single intraperitoneal injection of Aroclor 1254, 500 mg/kg, five days prior to sacrifice.

- S9 mix composition:

Component volume S9 100 µl

Sodium phosphate buffer 0.2M (pH 7.4) $500 \mu l$

 glucose 6 -phosphate
 5 μl

 N ADP 0.1 M
 40 μl

 KCI 1.65 M
 20 μl

 MgCl2 0.4
 20 μl

TEST ORGANISMS

- Salmonella typhimurium strains: TA98, TA100, TA1535, TA1537 and a 1538

- test organisms were properly maintained and were checked for appropriate genetic markers (rfa mutation, R factor)

TEST CONCENTRATIONS

(a) Preliminary cytotoxicity assay:

Plate incorporation assay: 0, 50, 144, 500, 1444 and 5000 µg per plate were evaluated without S9 activation with strains TA100 and TA 1538. Two plate was used, per dose, per condition.

(b)Mutation assays:

Plate incorporation assay: 0, 50, 166, 500, 1666 and 5000 µg per plate were evaluated in triplicate in the presence and absence of S9 activation; all test strains were used.

Test substance : Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Purity: no data

Conclusion: Dimethyldisulfide was negative in the Ames/Salmonella tester

strains TA1535, TA1537, TA1538, TA98 and TA100 with and without metabolic activation preparation over the dose range

 $50-5000 \mu g/plate$.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

31.12.2005 (27)

Type: Chromosomal aberration test

System of testing : Human Lymphocytes

Test concentration : 3.7; 11.1; 33.3; 100; 300 μg/ml

Cycotoxic concentr. : >= 300 µg/ml

Metabolic activation: with and withoutResult: ambiguous

Method : OECD Guide-line 473

Year : 1983 GLP : yes Test substance :

Method

: - Preliminary Cytotoxicity Assay:

The dose levels used in the chromosome aberration assay were established on the basis of the results of a preliminary toxicity test carried out with 6 concentrations of the test substance (ranging from 0.5 to 1000.0 μ g/ml), both in the absence and in the presence of the metabolic activation system (S -9 mix). The highest concentration for the toxicity test was determined by the limit of the solubility of the test substance in the tissue culture medium.

- Cytogenetic Assay:
- * Cell Treatment

After 48 h of incubation, the cultures were centrifuged. The cell pellets were resuspended in tissue culture medium supplemented with 20 mM HEPES (and 10% S-9 mix, for the test with metabolic activation) and appropriate test solutions. An untreated culture and a culture receiving DMSO served as negative controls. For each concentration of the test substance and for the controls one culture was used. Without S9, the cultures were incubated in closed tubes for another 24 hours including a 2 hour colcemid treatment. With S-9 mix, the exposure of the cells to the test substance was reduced to only 2 hours, because of the toxicity of the S-9 mix for the cells. After the 2 hour incubation period, the cells washed and supplied with freshly prepared culture medium. The cells were incubated for a further 22 hours (including a 2 hour colcimid treatment.

* Cell harvesting:

Two hours before the end of the total incubation period the cells were

arrested in the metaphase stage of the mitosis by the addition of colcemid. The cells were harvested, treated with a hypotonic solution, fixed three hours, and transferred to clean microscope slides. Two slides were prepared from each culture. The slides were stained 1000 stimulated lymphocytes were examined (500 from each slide) to determine the mitotic index (percentage of cells in mitosis).

* Metaphase analysis:

From each culture, 100 well-spread metaphases (each containing 46 chromosomes) were analysed by microscopic examination for a wide range of structural chromosome aberrations (gaps, breaks, fragments, dicentrics, exchanges etc.) and other anomalies (endoreduplication, polyploidy), according to the criteria recommended by Savage (1975).

- Evaluation criteria:

The major crite rion to designate the results of a chromosome aberration test as positive is a dose-related, statistically significant increase in the number of cells with structural chromosome aberrations. However, a clear dose-response relationship can be absent because the yield of chromosome aberrations can vary markedly with post-treatment sampling time of an asynchronous population and because increasing doses of clastogens can induce increasing degrees of mitotic delay. A test substance producing neither a dose-related,

statistically significant increase in the number of cells with structural chromosome aberrations, nor a statistically significant and reproducible positive response at any of the doses is considered non-clastogenic in this system.

Result : The test substance did not induce a statistically

significant increase in the number of cells with structural chromosome aberrations at non toxic concentrations, both in the absence and in the presence of the S-9 mix. At the very toxic concentration of 300.0 μ g/ml, both in the absence and

in the presence of the S-9 mix, the test substance induced a statistically

significant increase in the number of cells with structural chromosome aberrations.

The positive control substances, mitomycin C and cyclophosphamide, induced the expected increase in the incidence of structural chromosome aberrations.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : Control Materials:

Negative: DMSO

Solvent: The test article (dissolved in DMSO) was soluble in culture medium at a maximum concentration of 1 mg/mL Positive: -S9: mitomycin C (MMC) 0.05 µg/mL

+S9: cyclophosphamide (CP) 25 µg/mL

Activation:

S9 derived from adult male Wistar rats (Aroclor 1254 induced rat liver). The composition of the rat liver S9 reaction mix was: 8 mM magnesium chloride, 33 mM potassium chloride, 5 mM glucose-6-phosphate, 4 mM nicotinamide adenine dinucleotide phosphate (NADP), 100 mM sodium phospahte and 40% S9.

Culture Medium:

RPMI 1640 medium supplemented with heat-inactivated foetal calf serum, 100 units penicillin/mL, 100 µg streptomycin/mL, 2 mM L-glutamine and 25 µl phytohaemagglutinin/ml

100, 300

Test compound concentrations used:

of a factor of Discoult I for IC to

: Test substance: Dimethyl disulfide CAS no.: 624-92-0

Source: Atochem Purity: 99.98%

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Critical study for SIDS endpoint

31.12.2005 (14)

Type : Mammalian cell gene mutation assay

System of testing: HGPRT assay on CHO cells

Test concentration : 0.46; 1.37; 4.12; 12.3; 37.0; 74.0; 111; 333; 667 and 1000 μg/ml

Cycotoxic concentr. : 74.0-1000 µg/ml
Metabolic activation : with and without

Result : negative

Method : OECD Guide-line 476
Year : 1984

Year : 1984 GLP : yes Test substance :

Test substance

ld 624-92-0 5. Toxicity Date 31.12.2005

Method : The dose levels used in the HGPRT assay were established on

> the basis of the results of a preliminary solubility test. A final concentration of 1,000 µg/ml was chosen as highest

concentration for the HGPRT assays.

The two independent HGPRT-assays were carried out with

single cultures for each concentration of the test substance and for the

negative and positive controls.

In the absence of the S -9 mix, the test substance induced Result

neither a concentration-related increase in the mutant

frequency nor a reproducible positive response at one of the test

concentrations. In the presence of a metabolic

activation system, DMDS induced a slight increase in mutant frequency at several concentrations, in both HGPRT assays. These increases were neither concentration related nor clearly reproducible. In both HGPRT assays, the test substance appeared to be highly toxic to CHO cells at a

concentration range from 74.0-1,000 µg/ml.

The positive control substances, ethylmethanesulfonate and dimethylnitrosamine, induced the expected increase in the

mutant frequency.

: Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : - Control Materials:

* Negative: DMSO

* Solvent: The test article (dissolved in DMSO) was soluble in culture medium at a maximum concentration of 1 mg/mL

* Positive: -S9: Ethylmethanesulfonate 0.2 ml/L +S9: Dimethylnitrosamine 2 or 4 ml/L

- Activation:

S9 derived from adult male Wistar rats

- Culture Medium:

Ham's F-12 medium supplemented with 10% heat-inactivated foetal calf serum, 50 µg gentamicin/mL and 2 mM L-glutamine.

- Evaluation of the results:

The following criteria were used to evaluate the data obtained in the HGPRT assay (Li et al. 1987) a) the survival (absolute cloning efficiency) of the

negative controls should not be less than 50%,

b) the mean mutant frequency of the negative controls should fall within the range of 0-20 6-TG resistant mutants per 10e6 clonable cells.

- c) the positive controls must induce a response of a magnitude appropriate for the mutagen under the experimental conditions applied,
- d) the highest test substance concentration should, if possible, result in a clear cytotoxic response (e.g. 10-30% of the relative initial survival).

Any apparent increase in mutant frequency at concentrations of the test substance causing more than 90% toxicity is considered to be an artifact and not indicative of genotoxicity.

Genotoxicity of the test substance was evaluated using the following criteria (Li et al. 1987):

a) a concentration-related increase in mutant frequency, b) a reproducible positive response for at least one of the

test substance concentrations (e.g. the mean mutant

Source

frequency should be more than 20 mutants per 10e6 clonable

cells).

Test substance : Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Atochem Purity: 99.88%

Conclusion: No evidence for a genotoxic effect of DMDS was

found in cultured CHO cells, under the conditions used in

the HGPRT assay.

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Critical study for SIDS endpoint

31.12.2005

Type : DNA damage and repair assay
System of testing : Rat hepatocytes in primary culture
Test concentration : 1; 5; 10; 50; 100; 200 and 300 µg/ml

Cycotoxic concentr.: >= 100 μg/mlMetabolic activation: withoutResult: negative

Method : OECD Guide-line 482

Year : 1986 GLP : yes Test substance : other TS

Method : - Cytotoxicity evaluation:

The test compound cytotoxicity was assessed for both DNA

repair studies at the end of the treatment:

Each concentration of Dimethyldisulfide was tested in

triplicate.

- Autoradiography:

Autoradiographs were prepared by dipping slides in a photographic emulsion then developed. Slides were stained in

hematoxylin-phloxin.

- Slide assessment:

For each cell, following

nuclear grain court, cytoplasmic count was performed on 3 areas of the same size as the nucleus and adjacent to it.

- Data interpretation

The test compound is considered positive when the mean nuclear grain court is statistically greater than that of the control, the mean net nuclear grain court is above 3 grains per nucleus, and the percentage of treated cells in repair is significantly different from that of the controls. In addition, the effect must be shown to be reproducible

between experiments.

Result : Results

- Cytotoxic at 100, 200 and 300 µg/ml

IC50 evaluated by LDH release: 98 μg/ml (2nd study) - not genotoxic at concentrations of 10, 50, 100 and 200

µg/ml

The positive controls responded as expected.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : - Control Materials:

* Negative: pyrene 1 μM

* Solvent: DMSO

The test article was soluble in culture medium at a maximum

concentration of 100 µg/mL

* Positive:

. 7,12-DMBA (10 μM)

. 2-aminofluorene (0.1 and 0.5 µM)

- Number of cultures/concentration/study: 3

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Atochem Purity: 99.88%

Conclusion : Not genotoxic in vitro in the DNA repair test.

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Critical study for SIDS endpoint

31.12.2005 (16)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay

Species: mouseSex: male/femaleStrain: SwissRoute of admin.: inhalation

Exposure period : 6 h/day for 4 days **Doses** : 0, 250 and 500 ppm

Result : negative

Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"

Year : 1983 GLP : yes Test substance : other TS

Method : Three groups of mice were exposed during 6 hours a day for 4

consecutive days (days 0 through 3) to atmospheres

containing 0 ppn (5/sex), 250 ppm (5/sex) and 500 ppm DMDS

(10/sex).

The positive control group (5/sex) was treated once intraperitoneally, 24 hours before sacrifice, with 1.5 mg

Mitomycin C per kg body weight.

Bone marrow cells were collected from the femur and processed into smears for microscopic examination. One smear from each animal was examined for the presence of micronucleated poly- and normochromatic erythrocytes, (abbreviated MPE and MNE, respectively), and the total numbers of poly- and normochromatic erythrocytes (PE and NE) in a total of at least 2000 erythrocytes (E) in such a way that a minimum of 1000 PE

was observed.

Result: Exposure to DMDS resulted in clear signs of intoxication

both at the 250 ppm and the 500 ppm level. Mortality was observed in

some animals at 500 pmm group.

Exposure to 250 ppm and 500 ppm DMDS resulted in body weight loss

both in males and females.

There were no indications for increases in the incidences of MPE, MNE or

ME attributable to treatment with the test

material.

Mean numbers of PE per 1000 E were slightly lower in mice exposed to 500 ppm DMDS, both in males and females (0.001<P<0.01) pointing to slight cytotoxic effects on bone

marrow cells.

ld 624-92-0 5. Toxicity Date 31.12.2005

Animals treated with the mutagen Mitomycin C showed an

Atofina, Paris-la-Défense, France,

increased incidence of MPE.

Atofina Paris La Défense Cedex **Test condition** : * CONTROL MATERIALS

- Positive :

Mitomycin C, single ip administration, 1.5 mg/kg

: Test substance: D imethyl disulfide Test substance

> CAS no.: 624-92-0 Source: Atochem Purity: 99.88%

Conclusion It was concluded that the results of the micronucleus test

did not provide any indication of chromosomal damage and/or

damage to the mitotic apparatus in bone marrow cells of mice exposed to

DMDS.

Reliability (1) valid without restriction

Flag Material Safety Dataset, Critical study for SIDS endpoint

31.12.2005 (5)

Type Unscheduled DNA synthesis

Species : rat Sex male Strain Wistar Route of admin. inhalation **Exposure period** 4 hours Doses

Source

0 and 500 ppm

Result negative

other: OECD Guide-line 482 Method

Year 1986 **GLP** : ves Test substance other TS

Method Dimethyldisulfide (DMDS) was examined for its potential to

induce unscheduled DNA synthesis (UDS) in primary rat

hepatocytes after short-term exposure of male wistar rats to the test

substance by inhalation.

For the genotoxicity assay male rats were exposed by inhalation for a period of 4 h to one high concentration of 500 ppm DMDS (maximally tolerated concentration).

Immediately after exposure and after subsequent non-exposure periods of 16 and 24 h, animals were sacrificed for isolation of hepatocytes. The DNA-repair activities were examined by autoradiography in monolayer

cultures of hepatocytes, incubated in the presence of

[methyl-3H]thymidine.

The hepatocarcinogen 2-acetylaminofluorene (2 AAF), was used as a positive control in the in vivo/in vitro DNArepair assay and in the in vitro DNA-repair assay (2 AAF). Hepatocytes isolated from animals exposed to

air only served as negative controls.

Result DMDS did not induce DNA-repair activities in hepatocytes,

> either during the 4 h exposure period or during the subsequent 16 h or 24 h after the exposure period.

The positive control substance, 2-AAF, induced the expected

increase in DNA-repair activities. : Atofina, Paris-la-Défense, France, Atofina Paris La Défense Cedex

: * CONTROL MATERIALS **Test condition**

Source

- Positive :

. in vivo: 2-AAF, 50 mg/kg single oral administration

. in vitro: 2-AAF, 10e-4M

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Atochem Purity: 99.88%

Conclusion : It was concluded that DMDS did not induce DNA-repair in rat

hepatocytes.

Reliability : (1) valid without restriction

Flag : Material Safety Dataset, Critical study for SIDS endpoint

31.12.2005

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat Sex : female

Strain : other: Crl: CD(SD)BR

Route of admin. : inhalation

Exposure period : day 6 to day 15 of gestation

Frequency of treatm. : 6 h/day

Duration of test : up to gestation day 20

Doses : 5; 15; 50 ppm

Control group: yes, concurrent no treatment

NOAEL maternal tox. : = 5 ppm NOAEL teratogen. : = 50 ppm NOAEL Fetotoxicity : = 15 ppm

Method : OECD Guide-line 414 "Teratogenicity"

Year : 1981 GLP : yes Test substance :

Method : Three groups of 30 mated female rats were exposed to DMDS by

whole body exposure at 5, 15 or 50 ppm for 6 hours daily from day 6 to day 15 of gestation. A similar group of 30 rats, exposed to filtered air only over the same period, served as controls. All animals were maintained until day 20 of gestation, killed and their utering content assessed.

of gestation, killed and their uterine content assessed.

Result :

The chamber concentrations of the test article were close to target values throughout the exposure period. There were no deaths. A higher incidence of rough haircoat was observed at 50 ppm. Clinical condition at 5 and 15 ppm did not differ from controls. Dosage-related reductions in weight gain were observed at 15 and 50 ppm. Food intake was lower than controls at 50 ppm but comparable at 5 or 15 ppm.

No unusual lesions were observed at necropsy. There was no effect of

treatment on pre or post-implantation

loss, litter size or sex ratio. Litter and foetal weights

were reduced at 50 ppm. At 5 and 15 ppm these parameters were comparable to controls. No malformations were observed

in foetuses from the treated groups. A slightly higher incidence of retarded ossification was observed at 50 ppm but was considered to indicate delayed maturation, as a result of the lower foetal weight, rather than a teratogenic

effect.

Source : Atofina, Paris-la-Défense, France.

Atofina Paris La Défense Cedex

Test condition : TEST ORGANISMS:

- Number of animals: 100 rats: 25 females / dose group (3

dose groups + 1 control group)
- Aclimatation period: no data

ADMINISTRATION:

- Type of inhalation study: whole body

- Vehicle: filtered air

- Exposure chamber test article concentration

* Measured concentration

Samples for analysis were withdrawn from the exposure chambers twice hourly.

EXPERIMENTAL OBSERVATION

- Morbidity and mortality

All females were examined twice daily to detect any which were dead or moribund.

- Clinical observations

All females were examined daily from day 3 to day 20 of gestation. Any abnormalities of appearance or behaviour or other signs of reaction to treatment or ill health were recorded.

- Body weight

The body weight of each female was recorded

- Food intake

The amount of food consumed by each cage of females was recorded daily from day 3 to day 20 of gestation and reported on the body weight intervals.

- Terminal studies
- * Necropsy

All females were killed on day 20 of gestation, in random group order and examined macroscopically.

* Uterine/implantation data

pregnancy status

number of corpora lutea

number and intrauterine position of implantations

subdivided into:

live foetuses

early intrauterine deaths

late intrauterine deaths

dead foetuses

- Foetal data

Foetuses were weighed individually, examined externally and sexed. The viscera of approximately one half of the foetuses in each litter were examined. The skeleton was examined and preserved and stored in absolute glycerol (containing thymol crystals).

The remaining foetuses were placed in Bouin's fluid for at least two weeks then transferred to 70% industrial methylated spirit.

Foetal abnormalities were recorded as malformations (rare

and/or potentially lethal defects) and variations (cormnonly occurring non-

lethal abnormalities).

Test substance: Test substance: Dimethyl disulfide

C AS no.: 624-92-0 Source: Atochem Purity: 99.88%

Conclusion : Exposure to DMDS at 50 ppm elicited maternal toxicity, with

ld 624-92-0 5. Toxicity Date 31.12.2005

> associated fetal growth retardation (demonstrated by low weight and retarded ossification). There was no indication of a teratogenic effect. At 15 ppm, less marked maternal toxicity was observed and there were no fetal effects. There was no adverse effect of treatment, maternal or

fetal, at 5 ppm.

Reliability (1) valid without restriction

Material Safety Dataset, Critical study for SIDS endpoint Flag

31.12.2005 (3)

Species rat Sex female

Strain other: Crl: CD(SD)BR

Route of admin. inhalation

day 6 to day 15 of gestation Exposure period

Frequency of treatm. 6 h/day

Duration of test up to gestation day 20 **Doses** 10, 50 and 250 ppm

Control group yes, concurrent no treatment

NOAEL maternal tox. < 10 ppm other: range-finding study

Method

Year

yes GLP : Test substance other TS

Method Three groups of 7 time-mated female rats were exposed by

> inhalation (whole body) to concentrations of 10, 50 or 250 ppm of DMDS daily from day 6 to day 15 of gestation. A similar group of animals exposed to filtered air by the same route and over the same period acted as controls. All animals were maintained to day 20 of gestation when they

were killed and their uterine contents assessed.

Result All animals survived to day 20 of gestation. Comnon clinical signs were

observed at

an incidence which increased with dose, in the treated groups only. Dosage -related reductions in body weight gain were apparent in all treated groups over the exposure period. Dosage-related reductions in food intake were apparent in all treated groups over the exposure period. In the intermediate and high dose groups the lower intake

persisted until termination.

Pregnancy incidence was within the expected range in all groups. Pre-implantation loss was within the expected range in all treated groups. There was no adverse effect of treatment on the incidence of intrauterine deaths. Litter size was within the expected range in all treated groups. Sex ratio was within the expected range in all groups. Mean

litter weight was higher than controls in all treated

groups. Mean foetal weight showed a dosage -related reduction in the treated groups, but was considered an equivocal result as values for the control and low dose groups exceeded normal limits. No malformations

external examination of foetuses and the incidence of variations did not indicate an adverse effect of treatment.

Source : Atofina, Paris-la-Défense, France,

Atofina Paris La Défense Cedex

Test substance : Test substance: Dimethyl disulfide

CAS no.: 624-92-0 Source: Atochem Purity: 99.88%

Reliability : (1) valid without restriction

•	Date 31.12.2005
31.12.2005	(4)
5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES	
5.9 SPECIFIC INVESTIGATIONS	
5.10 EXPOSURE EXPERIENCE	
5.11 ADDITIONAL REMARKS	

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5. Toxicity

6. Analyt. Meth. for Detection and Identification

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- 6.1 ANALYTICAL METHODS
- 6.2 DETECTION AND IDENTIFICATION

7. Eff. Against Target Org. and Intended Uses

7.5

RESISTANCE

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7.1	FUNCTION
7.2	EFFECTS ON ORGANISMS TO BE CONTROLLED
7.3	OR GANISMS TO BE PROTECTED
7.4	USER

8. Meas. Nec. to Prot. Man, Animals, Environment

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8	.1	METHODS HANDLING AND STORING
8	.2	FIRE GUIDANCE
8	.3	EMERGENCY MEASURES
8	.4	POSSIB. OF RENDERING SUBST. HARMLESS
8	.5	WASTE MANAGEMENT
8	.6	SIDE-EFFECTS DETECTION
8	.7	SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER
Q	Q	DEACTIVITY TOWARDS CONTAINED MATERIAL

9. References Id 624-92-0 Date 31.12.2005

(1)	ATOCHEM. Ames metabolic activation test to assess the potential mutagenic effct of dimethyl disulphide. HRC report no. ATO 10/85427, 15 May 1985.
(2)	ATOCHEM. An in vivo/in vitro rat hepatocyte DNA-repair assay with dimethyldisulfide (DMDS). TNO-CIVO, Report V 90.082, May 1990.
(3)	ATOCHEM. Dimethyl Disulfide (DMDS), Inhalation Teratology Study in the Rat, Hazleton UK, Report 6205-514/9, December 1991.
(4)	ATOCHEM. DIMETH YL DISULFIDE (DMDS): Inhalation renge-finding study in the pregnant rat. Hazleton-UK study no. 6142-514/8, May 1991.
(5)	ATOCHEM. Examination of dimethyl disulfide in the micronucleus test, TNO-CIVO, Report V 89.366, October 1989.
(6)	ATOCHEM. Repeated-dose (28-day) dermal toxicity study with Dimethyl Disulfide (DMDS) in rabbits, TNO-CIVO Institutes, Report V 89.371/280554, February 1989.
(7)	BENTVELZEN, J.M. et al, 1975. Tappi, 58, 102-5. Kinetics of methyl mercaptan oxidation and dimethyl disulfide hydrolysis in alkaline solutions.
(8)	ELF ATOCHEM S.A., 1995.DIMETHYL DISULFURE.Détermination de la biodégradabilité facile.Essai en fioles fermées. Ref 95/SAEk/0415/NM.
(9)	Elf Atochem S.A., 2000.Centre d'application de Levallois. DISULFURE DE DIMETHYLE.Inhibition de la croissance des algues.Etude N° 504/99/A.
(10)	ELF ATOCHEM SA, 1996.DISULFURE DE DIMETHYLE. Toxicité aiguë vis-à-vis des daphnies.Rapport N°2606/95/A.
(11)	ELF ATOCHEM, DMDS: 90 day inhalation toxicity study in the rat with a 4 week recovery period, Hazelton UK, Report 6491-514/7, January 1992.
(12)	ELF ATOCHEM, Détermination de la toxicité par voie percutanée chez le lapin, Hazelton - IFT, Report 505207, 2 May 1985.
(13)	ELF ATOCHEM, In Vitro assay for the induction of point mutations in the HGPRTlocus of Chinese hamster ovary cells by dimethyldisulfide (DMDS), TNO-CIVO Institute, Report V 89.257, May 1990.
(14)	ELF ATOCHEM. Chromosome analysis of cultured human lymphocytes following in vitro treatment with DMDS. TNO-CIVO Institute, Report V 89.045, March 1990.
(15)	ELF ATOCHEM. DISULFURE DE DIMETHYLE. Tests de tolérance locale chez le lapin. Hazleton-IFT, Report 503398, 21 March 1985.

9. References Id 624-92-0 Pate 31.12.2005

(16)ELF ATOCHEM. In Vitro DNA Repair Test on Rat Hepatocytes in Primary Culture, SANOFI, Report RA860891026/PN1, 22 february 1990. ELF ATOCHEM. Repeated-dose (14-day) dermal toxicity (17)range-finding study with Dimethyl Disulfide (DMDS) in rabbits. TNO-CIVO Institutes, Report V 89.058/280553, July 1989. (18)Epiwin v 3.12, syspro experimental database EPIWIN v3.12 (19)Hansch, C et al. (1995) (20)(21)M.F. Tansy et al., Acute and Subchronic Toxicity studies of Rats Exposed to Vapors of Methyl Mercaptan and Other Reduced-Sulfur Compounds, J. Toxic. Environm. Health 1981, 8,71-88. (22)Pennwalt Corp. DIMETHYL DISULFIDE, EPA primary eye irritation. Products Safety Labs, Report T-5148, 24 June 1985. (23)Pennwalt Corp. DIMETHYL DISULFIDE, EPA primary skin irritation. Products Safety Labs, Report T-5149, June 24 1985. Pennwalt Corp. DIMETHYL DISULFIDE, Guinea pig sensitization (24)(Buehler). Products Safety Labs, Report T-5151, 30 August 1985. (25)Pennwalt Corp., DIMETHYL DISULFIDE. EPA acute dermal toxicity limit test. Products Safety Labs, Report T-5150, 24 June 1985. Pennwalt Corp., DIMETHYL DISULFIDE. EPA acute LD50. Products Safety Labs, Report (26)T-5147A, 14 August 1985. Pennwalt Corporation. DIMETHYL DISULFIDE, Ames (27)Salmonella/Microsome Plate Test (EPA/OECD). Pharmakon Research International, Inc. Report PH 301-PW-003-85, 31 May 1985. (28)Safety Data Sheet Elf Atochem January 1988 (29)SEPPOVAARA, O. and HYNNINEN, P., 1970. On the toxicity of sulfate -mill condensates. Papper och Trä, 1, 11-23. (30)SNEAP, Dimethyl disulfure (DMDS) - Evaluation de la toxicité aigüe chez le rat par voie orale, CIT Report 2064 TAR, June 1986. (31)Syracuse Research Corporation (SRC) and EPIWIN v 3.12. Technical Data Sheet A-1130-401 Elf Atochem January 1993 (32)(33)WERNER, A.E.: Sulphur compounds in kraft pulp mill effluents.Can. Pulp paper Ind., 1963, 16, 3, 35-43.

10. Summary and Evaluation

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10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT